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First Named Inventor:	MILLER, RICHARD L		
Application No.:	10/595117	Confirmation No.:	2906
Filed:	01-SEP-2004	Group Art Unit	1614
Title:	METHODS RELATED TO THE TREATMENT OF MUCOSAL ASSOCIATED CONDITIONS		

BRIEF ON APPEAL

Mail Stop: Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

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December 23, 2010 /Joyce M. Courtney/
Date Signed by: Joyce M. Courtney

Dear Sir:

This is an appeal from the Office Action mailed on June 24, 2010, in light of the Advisory Action mailed , finally rejecting claims 1-4, 7, 8, 11, 14, 17, 20-22, 27, 34 and 36.

Fees

☐ Any required fee under 37 CFR § 41.20(b)(2) will be made at the time of submission via EFS-Web. In the event fees are not or cannot be paid at the time of EFS-Web submission, please charge any fees under 37 CFR § 1.17 which may be required to Deposit Account No. 13-3723.

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A Notice of Appeal in this application was filed on September 23, 2010, and was received in the USPTO on September 23, 2010.

Appellants request the opportunity for a personal appearance before the Board of Appeals to argue the issues of this appeal. The fee for the personal appearance will be timely paid upon receipt of the Examiner's Answer.

REAL PARTY IN INTEREST

The real party in interest is 3M Company (formerly known as Minnesota Mining and Manufacturing Company) of St. Paul, Minnesota and its affiliate 3M Innovative Properties Company of St. Paul, Minnesota.

RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any related appeals or interferences.

STATUS OF CLAIMS

Claims 1-8, 11, 14, 17, 20-22, 27, 34, and 36 are pending. Claim 6 is withdrawn. Claims 1-4, 7-8, 11, 14, 17, 20-22, 27, 34 and 36 stand rejected.

STATUS OF AMENDMENTS

No amendments have been filed after the final rejection.

SUMMARY OF CLAIMED SUBJECT MATTER

Independent claim 1 concerns a method of delivering an immune response modifier (IRM) compound to a mucosal surface so as to achieve immunomodulation with reduced irritation of the mucosal surface from the IRM compound (page 2, lines 26-28), comprising interrupted delivery of an IRM compound other than imiquimod by intermittently applying in repeated applications the IRM to the mucosal surface (page 2, lines 29-30) and, after each application, removing from the mucosal surface (page 2, line 30, to page 3, line 1) at least 50% by weight of the IRM that was originally applied (page 5, lines 26-27) in each application at a time before it would otherwise be naturally absorbed or eliminated (page 3, lines 1-2).

Independent claim 2 concerns a method of treating a condition associated with a mucosal surface with an immune response modifier (IRM) compound and reducing irritation of the mucosal surface caused by the IRM (page 2, lines 26-28), comprising interrupted delivery of an IRM other than imiquimod by intermittently applying in repeated applications the IRM to the affected mucosal surface (page 2, lines 29-30) for a time sufficient to achieve therapeutic immunomodulation (page 2, lines 24-25) and, after each application, removing from the mucosal surface at least 50% of the IRM that was originally applied (page 5, lines 26-27) in each

application at a time before it would otherwise be naturally absorbed or eliminated (page 3, lines 1-2).

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 1-4, 7, 8, 11, 14, 17, 20-22, 27, 34 and 36 stand rejected under 35 USC § 103(a) as purportedly unpatentable over the combined teachings of US 2002/0058674 in view of WO 99/29693 in further view of US patent 6,328,991.

ARGUMENT

The claimed invention is based on the discovery that IRM compounds do not need to be left in place in order to be effective at inducing a substantial immune response, but can be applied intermittently for short intervals in order to "jump-start" the immune response and then removed so as to avoid unwanted side effects. This intermittent delivery-removal application regimen is not disclosed or suggested by any of the cited references and is particularly useful for application to mucosal tissues where irritation and unwanted systemic absorption can be significant problems.

As summarized in the specification:

> Although the beneficial effects of IRMs are known, the ability to provide therapeutic benefits via the topical application of an IRM compound to mucosal surfaces for the treatment of mucosal associated conditions is hindered. This is because of the resultant irritation of the mucosal surface that develops with extended contact with an IRM compound and because of undesired systemic delivery of the topically applied IRM compound.
>
> It has now surprisingly been found that the intermittent application of an IRM to a mucosal surface provides a therapeutic benefit without the irritation of the mucosal tissue associated with continuous (or extended) contact with the IRM. Thus, the present invention provides new methods for using IRM compounds to treat or prevent conditions associated with a mucosal surface. In some embodiments, the invention provides methods that are particularly advantageous for the topical application of an IRM to the cervix for treatment of cervical conditions such as cervical dysplasias including dysplasia associated with human papillomavirus (HPV), low-grade squamous intraepithelial lesions, high-grade squamous intraepithelial lesions, atypical squamous cells of undetermined significance (typically, with the presence of high-risk HPV), and cervical intraepithelial neoplasia (CIN).
>
> The present invention provides methods of reducing the irritation of a mucosal surface associated with treating a mucosal associated condition with an IRM. Alternatively stated, the present invention provides methods of delivering an IRM to a mucosal surface so as to achieve immunomodulation with reduced irritation.

Both independent claims 1 and 27 require intermittently applying an IRM other than imiquimod to a mucosal surface and, after each application, removing from the mucosal surface at least 50% by weight of the IRM that was originally applied before it would otherwise be

naturally absorbed or eliminated. This is not disclosed by any of the cited references and is not the same as using an applicator to delivery an IRM formulation and then removing the *applicator* (as opposed to the formulation).

With regard to US 2002/0058674, the Examiner observes that it discloses IRM compounds delivered to mucosal surfaces such as the cervix. The Examiner also observes that suppositories and applicators can be used for such delivery, but ignores that the delivery methods in US 2002/0058674 are designed to deliver and leave in place the IRM formulation (for 8 hours in the example using imiquimod). There is no indication that 50% of the IRM is removed after the 8 hours. While devices disclosed for delivery in the '674 would be removed after delivery, the Examiner points to no disclosure indicating that the IRM formulation is also removed with the applicator. To the contrary, it is clearly intended that the IRM is delivered from the applicator before applicator removal. Mucoadhesive is used in many of the formulations to improve residence time. Accordingly, the final rejection ignores the difference between conventionally removing a delivery applicator after the drug formulation has been deposited and the claimed invention where drug formulation itself must be removed. A reading of the '674 publication as a whole, including many of the passages recited by the Examiner, shows that the intention was to deliver the IRM formulations for an extended period of, e.g., 8 hrs and there was no suggestion of affirmative removal of at least 50% of the formulation from mucosal contact other than by natural clearance mechanisms.

The Examiner acknowledges that '674 is silent about removing at least 50% by weight of the IRM that was originally applied at a time before it would otherwise be naturally eliminated. However, Appellants further maintain that the '674 actually teaches away from the invention by (as noted in the Office Action) pointing out as a *problem* the potential for "wash away" of the IRM.

The Examiner cites WO 99/29693 for its disclosure of Appellants' elected species, which Appellants do not dispute.

The Examiner cites US patent 6,328,991 for its disclosure of a vaginal sponge for delivery various drugs (but not IRM compounds of the claimed invention), apparently for the proposition that such a sponge delivery device would or could involve application of a drug and

removal of at least 50% from the vaginal mucosal surface. However, the Examiner fails to explain where '991 discloses that a substantial amount of the drug is not delivered prior to removal from the vagina, or why one skilled in the art would combine '991 with the other cited references for use in a method that requires removing at least 50% of the IRM compound from the mucosal surface to which it was applied. It is apparent that '991 is using a vaginal sponge impregnated with a solution for the purpose of delivering (and leaving) the drug, not for initiating temporary contact with the mucosal tissue and then removing the drug.

Accordingly, it is submitted that the Examiner has failed to establish a prima facie case of obviousness of Claims 1 and 27 because (1) none of the references actually discloses or suggests applying and then removing at least 50% of the IRM, and (2) the Examiner provided no reasonable explanation as to why one skilled in the art would combine two references such as 2002/0058674 and US patent 6,328,991, having disclosures directed to conventionally delivering drugs intravaginally, to practice the claimed method of delivering and then removing at least 50% of the drug before it is otherwise naturally eliminated.

Applicants further submit that claim 11 is separately patentable since it calls for removal of at least 50% of the IRM within 2 hours after it is applied. None of the cited references suggest such a rapid removal interval or that an IRM drug would be effective using such method. The Examiner provides an insufficient explanation as to why such method would have been obvious, and merely speculates without support that one skilled in the art would desire to remove excess compound (providing nothing to suggest an amount of 50% within the claimed duration). The Examiner addresses the amount removed and the timing as "optimization", but fails to explain why one would have done so when it was not known that IRM compounds could quickly "jump-start" the immune system and then be removed to avoid unwanted side effects. The Examiner alludes to an absence of unexpected results, but Appellants submit that it was unexpected that IRM compounds would be effective when delivered for short intervals and then removed, and that such approach could be used to successfully reduce side effects.

Accordingly, it is submitted that a prima facie case of obviousness has not been established regarding claim 11 and, if established, has been rebutted by the surprising results disclosed in the application.

CONCLUSION

For the foregoing reasons, appellants respectfully submit that the Examiner has erred in rejecting this application. Please reverse the Examiner on all counts.

Respectfully submitted,

December 23, 2010
Date

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CLAIMS APPENDIX

1. (Previously Presented) A method of delivering an immune response modifier (IRM) compound to a mucosal surface so as to achieve immunomodulation with reduced irritation of the mucosal surface from the IRM compound, comprising:

interrupted delivery of an IRM compound other than imiquimod by intermittently applying in repeated applications the IRM to the mucosal surface and, after each application, removing from the mucosal surface at least 50% by weight of the IRM that was originally applied in each application at a time before it would otherwise be naturally absorbed or eliminated.

2. (Previously Presented) The method of claim 1 wherein the IRM is applied with a device and removed with the same device.

3. (Original) The method of claims 1 or 2 wherein the mucosal surface is associated with a condition selected from the group consisting of a cervical dysplasia, a papilloma virus infection of the cervix, a low-grade squamous intraepithelial lesion, a high-grade squamous intraepithelial lesion, atypical squamous cells of undetermined significance, a cervical intraepithelial neoplasia, an atopic allergic response, allergic rhinitis, a neoplastic lesion, and a premalignant lesion.

4. (Original) The method of claim 3 wherein the mucosal surface is on the cervix and the associated condition is selected from the group consisting of cervical dysplasia, high-grade squamous intraepithelial lesions, low-grade squamous intraepithelial lesions, and atypical squamous cells of undetermined significance with the presence of high risk HPV.

5. (Original) The method of claim 4 wherein the mucosal surface is on the cervix and the associated condition is atypical squamous cells of undetermined significance with the presence of high risk HPV.

6. (Withdrawn) The method of claim 3 wherein the mucosal surface is on the cervix and the associated condition is a papilloma virus infection of the cervix.

7. (Previously Presented) The method of any one of claims 1, 2, 4 through 6 wherein the IRM is applied to the mucosal surface using a device selected from the group consisting of a tampon, a cervical cap, a diaphragm, a cotton swab, a cotton sponge, a foam sponge, and a suppository.

8. (Previously Presented) The method of claim 1, wherein the at least 50% by weight of the IRM is removed less than 8 hours after it is applied.

9.-10. (Cancelled)

11. (Previously Presented) The method of claim 1 wherein the at least 50% by weight of the IRM is removed 2 hours or less after it is applied.

12.-13. (Cancelled)

14. (Previously Presented) The method of claim 1 wherein the IRM activates a TLR selected from the group consisting of TLR6, TLR7, TLR8, TLR 9, and combinations thereof.

15.- 16 (Cancelled)

17. (Previously Presented) The method of claim 1 wherein the IRM is selected from the group consisting of imidazoquinoline amines, tetrahydroimidazoquinoline amines, imidazopyridine amines, 6,7-fused cycloalkylimidazopyridine amines, 1,2-bridged imidazoquinoline amines, imidazonaphthyridine amines, imidazotetrahydronaphthyridine amines, oxazoloquinoline amines, thiazoloquinoline amines, oxazolopyridine amines, thiazolopyridine amines, oxazolonaphthyridine amines, thiazolonaphthyridine amines, 1*H*-imidazo dimers fused to pyridine amines, quinoline amines, tetrahydroquinoline amines, naphthyridine amines, or tetrahydronaphthyridine amines, pharmaceutically acceptable salts thereof, and combinations thereof.

18.-19. (Cancelled)

20. (Previously Presented) The method of claim 17 wherein the IRM is an imidazonaphthyridine amine or a pharmaceutically acceptable salt thereof.

21. (Original) The method of claim 20 wherein the IRM is 1-(2-methylpropyl)-1H-imidazo[4,5-c][1,5]naphthyridin-4-amine or a pharmaceutically acceptable salt thereof.

22. (Previously Presented) The method of claim 1 wherein the IRM comprises a 2-aminopyridine fused to a five membered nitrogen-containing heterocyclic ring.

23.-26. (Cancelled)

27. (Previously Presented) A method of treating a condition associated with a mucosal surface with an immune response modifier (IRM) compound and reducing irritation of the mucosal surface caused by the IRM, comprising:

interrupted delivery of an IRM other than imiquimod by intermittently applying in repeated applications the IRM to the affected mucosal surface for a time sufficient to achieve therapeutic immunomodulation and, after each application, removing from the mucosal surface at least 50% of the IRM that was originally applied in each application at a time before it would otherwise be naturally absorbed or eliminated.

28.-33. (Cancelled)

34. (Previously Presented) The method of claim 27 wherein the IRM is predispersed within a solid matrix capable of releasing the IRM while in contact with the mucosal surface.

35. (Cancelled)

36. (Previously Presented) The method of claim 34 wherein the solid matrix is selected from the group consisting of a tampon, a sponge, and a suppository.

37.-40. (Cancelled)

EVIDENCE APPENDIX

None.

RELATED PROCEEDINGS APPENDIX

None.